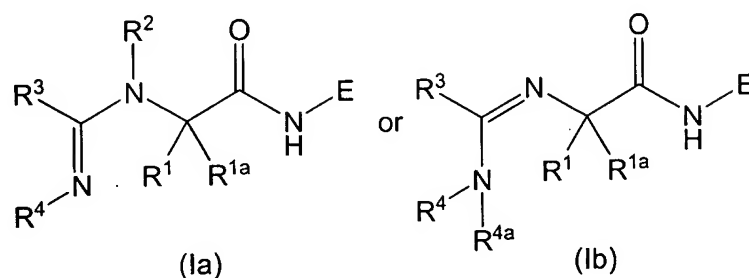


Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1. (Original) A compound of Formula (Ia) or (Ib):



wherein:

E is:

(i) $-C(R^5)(R^6)X^1$ where X^1 is $-CHO$, $-C(R^7)(R^8)CF_3$,
 $-C(R^7)(R^8)CF_2CF_2R^9$, $-C(R^7)(R^8)R^{10}$, $-CH=CHS(O)_2R^{10}$, $-C(R^7)(R^8)C(R^7)(R^8)OR^{10}$,
 $-C(R^7)(R^8)CH_2OR^{10}$, $-C(R^7)(R^8)C(R^7)(R^8)R^{10}$, $-C(R^7)(R^8)CH_2N(R^{11})SO_2R^{10}$,
 $-C(R^7)(R^8)CF_2C(O)NR^{10}R^{11}$, $-C(R^7)(R^8)C(O)NR^{10}R^{11}$, $-C(R^7)(R^8)C(O)N(R^{11})$,
 $(CH_2)_2OR^{11}$, or $-C(R^7)(R^8)C(O)N(R^{11})(CH_2)_2NHR^{11}$;

where:

R^5 is hydrogen or (C_{1-6}) alkyl;

R^6 is hydrogen, (C_{1-6}) alkyl, cyano, $-X^2NR^{12}R^{12a}$, $-X^2NR^{12}C(O)R^{12a}$,
 $-X^2NR^{12}C(O)OR^{12a}$, $-X^2NR^{12}C(O)NR^{12a}R^{12b}$, $-X^2NR^{12}C(N^{12a})NR^{12b}R^{12c}$, $-X^2OR^{13}$, $-X^2SR^{13}$,
 $X^2C(O)OR^{12}$, $-X^2C(O)R^{13}$, $-X^2OC(O)R^{13}$, $-X^2C(O)NR^{12}R^{12a}$, $-X^2S(O)_2NR^{12}R^{12a}$,
 $-X^2NR^{12}S(O)_2R^{13}$, $-X^2P(O)(OR^{12})OR^{12a}$, $-X^2OP(O)(OR^{12})OR^{12a}$, $-X^2S(O)R^{14}$, $-X^2S(O)_2R^{14}$, R^{15} ,
 $-X^2OR^{15}$, $-X^2SR^{15}$, $-X^2S(O)R^{15}$, $-X^2S(O)_2R^{15}$, $-X^2C(O)R^{15}$, $-X^2C(O)OR^{15}$, $-X^2OC(O)R^{15}$,
 $-X^2NR^{15}R^{12}$, $-X^2NR^{12}C(O)R^{15}$, $-X^2NR^{12}C(O)OR^{15}$, $-X^2C(O)NR^{15}R^{12}$, $-X^2S(O)_2NR^{15}R^{12}$,

$X^2NR^{12}S(O)_2R^{15}$, $-X^2NR^{12}C(O)NR^{15}R^{12a}$ or $-X^2NR^{12}C(NR^{12a})NR^{15}R^{12}$ where X^2 is (C_{1-6}) alkylene; R^{12} , R^{12a} , R^{12b} and R^{12c} at each occurrence independently is hydrogen or (C_{1-6}) alkyl; R^{13} is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, R^{14} is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl; and R^{15} is (C_{3-10}) cycloalkyl (C_{0-6}) alkyl, hetero (C_{3-10}) cycloalkyl (C_{0-3}) alkyl, (C_{6-10}) aryl (C_{0-6}) alkyl, hetero (C_{5-10}) aryl (C_{0-6}) alkyl, (C_{9-12}) bicycloaryl (C_{0-6}) alkyl or hetero (C_{8-12}) bicycloaryl (C_{0-6}) alkyl; or

R^5 and R^6 taken together with the carbon atom to which both R^5 and R^6 are attached form (C_{3-8}) cycloalkylene or hetero (C_{3-8}) cycloalkylene wherein said cycloalkylene and heterocycloalkylene may be substituted further with 1 to 2 radicals independently selected from (C_{1-6}) alkyl, cyano, halo, halo-substituted (C_{1-4}) alkyl, nitro, $-X^3NR^{16}R^{16a}$, $X^3N^{16}C(O)R^{16a}$, $-X^3NR^{16}C(O)OR^{16a}$, $-X^3NR^{16}C(O)NR^{16a}R^{16b}$, $-X^3NR^{16}C(NR^{16a})NR^{16b}R^{16c}$, X^3OR^{17} , $-X^3SR^{17}$, $-X^3C(O)OR^{16}$, $-X^3C(O)R^{17}$, $-X^3OC(O)R^{17}$, $-X^3C(O)NR^{16}R^{16a}$, $X^3S(O)_2NR^{16}R^{16a}$, $-X^3NR^{16}S(O)_2R^{17}$, $-X^3P(O)(OR^{16})OR^{16a}$, $-X^3OP(O)(OR^{16})OR^{16a}$, $X^3S(O)R^{18}$ and $-X^3S(O)_2R^{18}$ where X^3 is a bond or (C_{1-6}) alkylene; R^{16} , R^{16a} , R^{16b} , and R^{16c} at each occurrence independently is hydrogen or (C_{1-6}) alkyl; R^{17} is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl, and R^{18} is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl;

R^7 is hydrogen or (C_{1-4}) alkyl;

R^8 is hydroxy; or

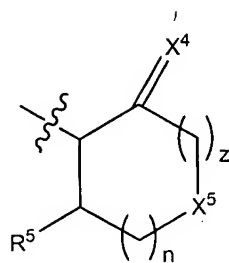
R^7 and R^8 together form oxo;

R^9 is hydrogen, halo, (C_{1-4}) alkyl, (C_{5-10}) aryl (C_{0-6}) alkyl or hetero (C_{5-10}) aryl (C_{0-6}) alkyl; and

R^{10} is (C_{1-4}) alkyl, (C_{6-10}) aryl (C_{0-6}) alkyl, hetero (C_{4-10}) aryl (C_{0-6}) alkyl, (C_{4-10}) cycloalkyl (C_{0-6}) alkyl or hetero (C_{4-10}) cycloalkyl (C_{0-6}) alkyl; and

R^{11} is hydrogen or (C_{1-6}) alkyl; or

(ii) a group of formula (a):



(a)

(a)

where:

n is 0, 1, or 2;

z is 0 or 1;

X⁴ is selected from NR¹⁹, S, or 0 where R¹⁹ is hydrogen or (C₁₋₆)alkyl; and

X⁵ is -O-, -S-, -SO₂-, or -NR²⁰ - where R²⁰ is selected from hydrogen, (C₁₋₆)alkyl, X⁶C(O)OR²², -X⁶C(O)NR²²R^{22a}, -X⁶S(O)₂NR²²R^{22a}, -X⁶C(O)R²³, -X⁶S(O)₂R²⁴, -R²⁵, -X⁶C(O)OR²⁵, -X⁶C(O)NR²²R²⁵, -X⁶S(O)₂NR²²R²⁵, -X⁶C(O)R²⁵ and -X⁶S(O)₂R²⁵ in which X⁶ is a bond or (C₁₋₆)alkylene; R²² and R^{22a} at each occurrence independently is hydrogen or (C₁₋₆)alkyl; R²³ is hydrogen, (C₁₋₆) alkyl or halo-substituted(C₁₋₆)alkyl, R²⁴ is (C₁₋₆)alkyl or halo-substituted(C₁₋₆) alkyl, and R²⁵ is (C₃₋₁₀)cycloalkyl(C₀₋₆) alkyl, hetero(C₃₋₁₀)cycloalkyl(C₀₋₃)alkyl, (C₆₋₁₀)aryl(C₀₋₆)alkyl, hetero(C₅₋₁₀)aryl(C₀₋₆)alkyl, (C₉₋₁₂)bicycloaryl(C₀₋₆)alkyl or hetero(C₈₋₁₂)bicycloaryl(C₀₋₆)alkyl provided that when R⁵ is hydrogen, then both X⁴ and X⁵ are not -O-;

R⁵ is as defined above;

and furthermore within E any cycloalkyl, heterocycloalkyl, aryl or heteroaryl may be substituted with R^x selected from -R²⁶, -X⁷OR²⁶, -X⁷SR²⁶, -X⁷S(O)R²⁶, -X⁷S(O)₂R²⁶, -X⁷C(O)R²⁶, -X⁷C(O)OR²⁶, -X⁷OC(O)R²⁶, -X⁷NR²⁶R²⁷, -X⁷NR²⁷C(O)R²⁶, -X⁷NR²⁷C(O)OR²⁶, X⁷C(O)NR²⁶R²⁷, -X⁷S(O)₂NR²⁶R²⁷, -X⁷NR²⁷S(O)₂R²⁶, -X⁷NR²⁷C(O)NR²⁶R^{27a} and

$-X^7NR^{27}C(NR^{27a})NR^{26}R^{27b}$ and wherein E and R^x may be substituted further with 1 to 5 radicals independently selected from (C₁₋₆)alkyl, cyano, halo, halo-substituted(C₁₋₄)alkyl, nitro, $-X^8NR^{28}R^{28a}$, $-X^8NR^{28}C(O)R^{28a}$, $-X^8NR^{28}C(O)OR^{28a}$, $-X^8NR^{28}C(O)NR^{28a}R^{28b}$, $X^8NR^{28}C(NR^{28a})NR^{28b}R^{28c}$, $-X^8OR^{29}$, $-X^8SR^{29}$, $-X^8C(O)OR^{28}$, $-X^8C(O)R^{29}$, $-X^8OC(O)R^{29}$, $-X^8C(O)NR^{28}R^{28a}$, $-X^8S(O)_2NR^{28}R^{28a}$, $-X^8NR^{28}S(O)_2R^{29}$, $-X^8P(O)(OR^{28})OR^{28a}$, $-X^8OP(O)(OR^{28})OR^{28a}$, $-X^8S(O)R^{30}$ and $-X^8S(O)_2R^{30}$ wherein X^7 and X^8 are independently a bond or (C₁₋₆)alkylene; R^{26} is (C₃₋₁₀)cycloalkyl(C₀₋₆)alkyl, hetero(C₃₋₁₀)cycloalkyl(C₀₋₃)alkyl, (C₆₋₁₀)aryl(C₀₋₆)alkyl, hetero(C₅₋₁₀)aryl(C₀₋₆)alkyl, (C₉₋₁₂)bicycloaryl(C₀₋₆)alkyl or hetero(C₈₋₁₂)bicycloaryl(C₀₋₆)alkyl, R^{27} , R^{27a} , R^{27b} , R^{28} , R^{28a} , R^{28b} and R^{28c} at each occurrence independently is hydrogen or (C₁₋₆)alkyl, R^{29} is hydrogen, (C₁₋₆)alkyl or halo-substituted(C₁₋₆)alkyl, and R^{30} is (C₁₋₆)alkyl or halo-substituted(C₁₋₆)alkyl;

R^1 is (C₁₋₁₀)alkyl or $-C(R^{31})(R^{32})X^9$ wherein R^{31} and R^{32} are independently hydrogen or (C₁₋₆)alkyl and X^9 is selected from $-X^{10}NR^{33}R^{33a}$, $-X^{10}NR^{33}C(O)R^{33a}$, $-X^{10}NR^{33}C(O)OR^{33a}$, $X^{10}NR^{33}C(O)NR^{33a}R^{33b}$, $-X^{10}NR^{33}C(NR^{33a})NR^{33b}R^{33c}$, $-X^{10}OR^{33}$, $-X^{10}SR^{33}$, $-X^{10}C(O)OR^{33}$, $-X^{10}C(O)R^{33}$, $-X^{10}OC(O)R^{33}$, $-X^{10}C(O)NR^{33}R^{33a}$, $-X^{10}S(O)_2NR^{33}R^{33a}$, $-X^{10}NR^{33}S(O)_2R^{33a}$, $X^{10}P(O)(OR^{33})OR^{33a}$, $-X^{10}OP(O)(OR^{33})OR^{33a}$, $-X^{10}C(O)R^{34}$, $-X^{10}NR^{33}C(O)R^{34}$, $-X^{10}S(O)R^{34}$, $X^{10}S(O)_2R^{34}$, $-R^{35}$, $-X^{10}OR^{35}$, $-X^{10}SR^{35}$, $-X^{10}S(O)R^{35}$, $-X^{10}S(O)_2R^{35}$, $-X^{10}C(O)R^{35}$, $-X^{10}C(O)OR^{35}$, $-X^{10}OC(O)R^{35}$, $-X^{10}NR^{33}R^{35}$, $-X^{10}NR^{33}C(O)R^{35}$, $-X^{10}NR^{33}C(O)OR^{35}$, $-X^{10}C(O)NR^{33}R^{35}$, $-X^{10}S(O)_2NR^{33}R^{35}$, $-X^{10}NR^{33}S(O)_2R^{35}$, $-X^{10}NR^{33}C(O)NR^{33a}R^{35}$ and $-X^{10}NR^{33}C(NR^{33a})NR^{33b}R^{35}$ wherein X^{10} is a bond or (C₁₋₆)alkylene; R^{33} , R^{33a} , R^{33b} , and R^{33c} at each occurrence independently is hydrogen, (C₁₋₆)alkyl or halo-substituted(C₁₋₆)alkyl; R^{34} is (C₁₋₆)alkyl or halo-substituted(C₁₋₆)alkyl; and R^{35} is (C₃₋₁₀)cycloalkyl(C₀₋₆)alkyl, hetero(C₃₋₁₀)cycloalkyl(C₀₋₃)alkyl, (C₆₋₁₀)aryl(C₀₋₆)alkyl, hetero(C₅₋₁₀)aryl(C₀₋₆)alkyl, (C₉₋₁₀)bicycloaryl(C₀₋₆)alkyl or hetero(C₈₋₁₀)bicycloaryl(C₀₋₆)alkyl;

wherein within R^1 any alicyclic or aromatic ring system is unsubstituted or substituted further by 1 to 5 radicals independently selected from (C₁₋₆)alkyl, (C₁₋₆)alkylidene, cyano, halo, halo-substituted(C₁₋₄)alkyl, nitro, $-X^{11}NR^{36}R^{36a}$, $-X^{11}NR^{36}C(O)R^{36a}$, $-X^{11}NR^{36}(O)OR^{36a}$, $-X^{11}NR^{36}C(O)NR^{36a}R^{36b}$, $-X^{11}NR^{36}C(NR^{36a})NR^{36b}R^{36c}$, $-X^{11}OR^{36}$, $X^{11}SR^{36}$,

$-X^{11}C(O)OR^{36}$, $-X^{11}C(O)R^{36}$, $-X^{11}OC(O)R^{36}$, $-X^{11}C(O)NR^{36}R^{36a}$, $X^{11}S(O)_2NR^{36}R^{36a}$,
 $-X^{11}NR^{36}S(O)_2R^{36a}$, $-X^{11}P(O)(OR^{36})OR^{36a}$, $-X^{11}OP(O)(OR^{36})OR^{36a}$, $X^{11}NR^{36}C(O)R^{37}$,
 $-X^{11}S(O)R^{37}$, $-X^{11}C(O)R^{37}$ and $-X^{11}S(O)_2R^{37}$ and/or 1 radical selected from $-R^{38}$, $-X^{12}OR^{38}$,
 $-X^{12}SR^{38}$, $-X^{12}S(O)R^{38}$, $-X^{12}S(O)_2R^{38}$, $-X^{12}C(O)R^{38}$, $-X^{12}C(O)OR^{38}$, $X^{12}OC(O)R^{38}$,
 $X^{12}NR^{36}R^{38}$, $-X^{12}NR^{36}C(O)R^{38}$, $-X^{12}NR^{36}C(O)OR^{38}$, $-X^{12}C(O)NR^{36}R^{38}$, $X^{12}S(O)_2NR^{36}R^{38}$,
 $-X^{12}NR^{36}S(O)_2R^{38}$, $-X^{12}NR^{36}C(O)NR^{36a}R^{38}$ and $-X^{12}NR^{36}C(N^{36a})NR^{36b}R^{38}$; and within R^1 any
aliphatic moiety is unsubstituted or substituted further by 1 to 5 radicals independently selected
from cyano, halo, nitro, $-NR^{39}R^{39a}$, $N^{39}C(O)R^{39a}$, $-NR^{39}C(O)OR^{39a}$, $-NR^{39}C(O)NR^{39a}R^{39b}$,
 $-NR^{39}C(NR^{39a})NR^{39b}R^{39c}$, $-OR^{39}$, $-SR^{39}$, $-C(O)OR^{39}$, $-C(O)R^{39}$, $-OC(O)R^{39}$, $-C(O)NR^{39}R^{39a}$,
 $-S(O)_2NR^{39}R^{39a}$, $-NR^{39}S(O)_2R^{39a}$, $-P(O)(OR^{39})OR^{39a}$, $-OP(O)(OR^{39})OR^{39a}$, $-NR^{39}C(O)R^{40}$,
 $-S(O)R^{40}$ and $-S(O)_2R^{40}$; wherein X^{11} and X^{12} are independently a bond or (C_{1-6}) alkylene; R^{36} ,
 R^{36a} , R^{36b} , R^{36c} , R^{39} , R^{39a} , R^{39b} and R^{39c} at each occurrence independently is hydrogen, (C_{1-6}) alkyl
or halo-substituted (C_{1-6}) alkyl; R^{37} and R^{40} are independently (C_{1-6}) alkyl or halo-
substituted (C_{1-6}) alkyl; and R^{38} is (C_{3-10}) cycloalkyl (C_{0-6}) alkyl, hetero (C_{3-10}) cycloalkyl (C_{0-3}) alkyl,
 (C_{6-10}) aryl (C_{0-6}) alkyl, hetero (C_{5-10}) aryl (C_{0-6}) alkyl, (C_{9-10}) bicycloaryl (C_{0-6}) alkyl or
hetero (C_{6-10}) bicycloaryl (C_{0-6}) alkyl, provided that only one (C_{9-10}) bicycloaryl (C_{0-6}) alkyl or
hetero (C_{8-10}) bicycloaryl (C_{0-6}) alkyl ring structure is present within R^1 ;

R^{1a} is hydrogen or (C_{1-6}) alkyl; or

R^1 and R^{1a} together with the carbon atoms to which they are attached form
 (C_{3-8}) cycloalkylene or hetero (C_{3-10}) cycloalkylene ring wherein said cycloalkylene ring is
optionally substituted with one or two substituents independently selected from (C_{1-6}) alkyl,
 (C_{1-6}) alkoxy, hydroxy, halo, hydroxyalkyl, or keto and said heterocycloalkylene ring is
optionally substituted with one or two substituents independently selected from (C_{1-6}) alkyl,
 (C_{1-4}) alkoxy, hydroxyalkyl, alkoxyalkyl, aminoalkyl, acyl, (C_{3-10}) cycloalkyl (C_{0-6}) alkyl,
hetero (C_{3-10}) cycloalkyl (C_{0-3}) alkyl, (C_{6-10}) aryl (C_{0-6}) alkyl, hetero (C_{5-10}) aryl (C_{0-6}) alkyl wherein said
aryl, heteroaryl, and heterocycloalkyl are optionally substituted with one, two, or three
substituents independently selected from (C_{1-4}) alkyl, (C_{1-6}) alkoxy, nitro, amino, halo, hydroxy,

alkylthio, halo-substituted alkyl, halo-substituted alkoxy, acyl, $-\text{OC}(\text{O})\text{R}^{39}$, $-\text{C}(\text{O})\text{NR}^{39}\text{R}^{39a}$, $-\text{S}(\text{O})_2\text{NR}^{39}\text{R}^{39a}$, $-\text{S}(\text{O})_2\text{R}^{38}$ or $-\text{S}(\text{O})_2\text{R}^4$ where R^{38} , R^{39} , R^{39a} , and R^4 are as defined above;

R^2 is hydrogen, hydroxy, or (C_{1-6}) alkyl;

R^3 is hydrogen, (C_{1-6}) alkyl, (C_{1-6}) alkoxy, aryloxy, (C_{3-8}) cycloalkyl, (C_{3-8}) cycloalkyloxy, aryl, benzyl, tetrahydronaphthyl, indenyl, indanyl, (C_{1-6}) alkylsulfonyl (C_{1-6}) alkyl, (C_{3-8}) cycloalkylsulfonyl (C_{1-6}) alkyl, arylsulfonyl (C_{1-6}) alkyl, heterocyclic ring selected from azepanyl, azocanyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl, tetrahydropyranyl, tetrahydrothiopyranyl, thiopyranyl, furanyl, tetrahydrofuranyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, tetrazolyl, pyrazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzisoxazolyl, quinolinyl, tetrahydroquinolinyl, isoquinolinyl, tetrahydroisoquinolinyl, quinazolinyl, tetrahydroquinazolinyl, benzoxazolyl or quinoxalinyl, $-\text{OR}$ where R is a heterocyclic moiety selected from those herein described in this paragraph, or amino; wherein R^3 is optionally substituted by one, two, or three R^a ;

each R^a is independently (C_{1-6}) alkyl, (C_{3-8}) cycloalkyl, aryl, tetrahydronaphthyl, indenyl, indanyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, benzisoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, (C_{1-6}) alkoxy, (C_{1-6}) haloalkoxy, (C_{1-6}) alkanoyl, (C_{1-6}) alkanoyloxy, aryloxy, benzyloxy, (C_{1-6}) alkoxycarbonyl, aryloxycarbonyl, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by (C_{1-6}) alkyl, aryl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl or quinoxalinyl, or

each R^a is independently (C₁₋₆)alkanoylamino, aroylamino, (C₁₋₆)alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by (C₁₋₆)alkyl, aryl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl or quinoxalinyl, or

each R^a is independently (C₁₋₆)alkoxycarbonylamino, aryloxycarbonylamino, (C₁₋₆)alkylcarbamoyloxy, arylcarbamoyloxy, (C₁₋₆)alkylsulfonylamino, arylsulfonylamino, aminosulfonyl, (C₁₋₆)alkylaminosulfonyl, di-(C₁₋₆)alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by (C₁₋₆)alkyl, aryl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl or quinoxalinyl, or

each R^a is independently halogen, hydroxy, (C₁₋₆)alkoxy, (C₁₋₆)haloalkyl, (C₁₋₆)haloalkoxy, oxo, carboxy, cyano, nitro, carboxamide, amidino or guanidino, R^a is may be further optionally substituted by one, two, or three R^b;

each R^b is independently (C₁₋₆)alkyl optionally partially or fully halogenated wherein one or more carbon atoms are optionally replaced by O, N, S(O), S(O)₂ or S and wherein said alkyl is optionally independently substituted with 1-2 oxo groups, -NH₂, or one or more C₁₋₄ alkyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, or quinoxalinyl; or

each R^b is independently (C₁₋₆)cycloalkyl, aryl, aryloxy, benzyloxy, halogen, hydroxy, (C₁₋₆)alkyl, (C₁₋₆)alkoxy, (C₁₋₆)haloalkyl, (C₁₋₆)haloalkoxy, aminosulfonyl,

(C₁₋₆)alkylaminosulfonyl, di-(C₁₋₆)alkylaminosulfonyl, arylaminosulfonyl, oxo, carboxy, cyano, nitro, mono-C₁₋₅alkylamino, di-(C₁₋₅)alkylamino, carboxamide, amidino or guanidino;

R⁴ is hydrogen, hydroxy, nitrile, or a (C₁₋₆)alkyl optionally partially or fully halogenated wherein one or more C atoms are optionally replaced by O, NH, S(O), S(O)₂ or S and wherein said alkyl chain is optionally independently substituted with 1-2 oxo groups, -NH₂, one or more C₁₋₄ alkyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl, thiopyranyl, furanyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, benzoxazolyl or quinoxalinyl; or

R³ and R⁴ together with the atoms to which they are attached form a heterocycloalkyl ring or a heterocyclic ring fused to an aryl or heteroaryl ring provided that the heterocycloalkyl rings contain at least an -SO₂- group, wherein said heterocycloalkyl rings may be optionally substituted on the aromatic and/or non-aromatic portion of the rings with one, two, or three R^c;

each R^c and R^{4a} is independently:

hydrogen, (C₁₋₆)alkyl optionally interrupted by one or two N, O, S, S(O), or S(O)₂ and optionally substituted by 1-2 oxo, amino, hydroxy, halogen, C₁ alkyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl, thiopyranyl, furanyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, benzoxazolyl or quinoxalinyl;

halo, alkoxy, alkylthio, hydroxy, carboxy, aryl, aryloxy, aroyl, heteroaryl, (C₁₋₆)alkanoyl, -C(O)OR^d where (R^d is hydrogen, (C₁₋₆)alkyl, (C₁₋₆)alkoxyalkyl, (C₁₋₆)haloalkyl, (C₃₋₇)cycloalkyl, (C₃₋₇)cycloalkyl(C₁₋₆)alkyl, heteroaryl, heteroaryl(C₁₋₆)alkyl, aryl, or aryl(C₁₋₆)alkyl), (C₁₋₆)alkylsulfonyl, aryloxycarbonyl, benzyloxycarbonyl, (C₁₋₆)alkanoylamino, aroylamino, C₁₋₅ alkylthio, arylthio, (C₁₋₆)alkylsulfonylamino, arylsulfonylamino,

(C₁₋₆)alkylamino-sulfonyl, arylaminosulfonyl, (C₃₋₆)cycloalkyl and benzyloxy wherein each of the aforementioned group is optionally substituted with halogen, hydroxy, (C₁₋₆)alkyl, (C₁₋₆)alkoxy, (C₁₋₆)haloalkyl, (C₁₋₆)haloalkoxy, oxo, carboxy, nitrile, nitro or NH₂C(O)-; or a pharmaceutically acceptable salts thereof provided that there are no more than 5 ring systems in a compound of Formula (Ia) or (Ib).

2. (Original) The compound of Claim 1 wherein:

R³ is (C₁₋₆)alkyl, (C₁₋₆)alkoxy, aryloxy, (C₃₋₈)cycloalkyl, (C₃₋₈)cycloalkyloxy, aryl, benzyl, tetrahydronaphthyl, indenyl, indanyl, (C₁₋₆)alkylsulfonyl(C₁₋₆)alkyl, (C₃₋₈)cycloalkylsulfonyl(C₁₋₆)alkyl, arylsulfonyl(C₁₋₆)alkyl, heterocyclic ring selected from azepanyl, azocanyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl, tetrahydropyranyl, tetrahydrothiopyranyl, thiopyranyl, furanyl, tetrahydrofuranyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, tetrazolyl, pyrazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzisoxazolyl, quinolinyl, tetrahydroquinolinyl, isoquinolinyl, tetrahydroisoquinolinyl, quinazolinyl, tetrahydroquinazolinyl, benzoxazolyl or quinoxalinyl, -OR where R is a heterocyclic moiety selected from those herein described in this paragraph, or amino; wherein R³ is optionally substituted by one, two, or three R^a;

each R^a is independently (C₁₋₆)alkyl, (C₃₋₈)cycloalkyl, aryl, tetrahydronaphthyl, indenyl, indanyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, benzisoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, (C₁₋₆)alkoxy, (C₁₋₆)haloalkoxy, (C₁₋₆)alkanoyl, (C₁₋₆)alkanoyloxy, aryloxy, benzyloxy, (C₁₋₆)alkoxycarbonyl, aryloxycarbonyl, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by (C₁₋₄)alkyl, aryl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl or quinoxalinyl, or each

R^a is independently (C₁₋₆)alkanoylamino, aroylamino, (C₁₋₆)alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureid'o wherein either nitrogen atom may be independently substituted by (C₁₋₆)alkyl, aryl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl or quinoxalinyl, or

each R^a is independently (C₁₋₆)alkoxycarbonylamino, aryloxycarbonylamino, (C₁₋₆)alkylcarbamoyloxy, arylcarbamoyloxy, (C₁₋₆)alkylsulfonylamino, arylsulfonylamino, aminosulfonyl, (C₁₋₆)alkylaminosulfonyl, di-(C₁₋₆)alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by (C₁₋₆)alkyl, aryl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl or quinoxalinyl, or

each R^a is independently halogen, hydroxy, (C₁₋₆)alkoxy, (C₁₋₆)haloalkyl, (C₁₋₆)haloalkoxy, oxo, carboxy, cyano, nitro, carboxamide, amidino or guanidino, R^a is may be further optionally substituted by one, two, or three R^b ;

each R^b is independently (C₁₋₆)alkyl optionally partially or fully halogenated wherein one or more carbon atoms are optionally replaced by O, N, S(O), S(O)₂ or S and wherein said alkyl is optionally independently substituted with 1-2 oxo groups, -NH₂, or one or more C₁₋₄ alkyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, or quinoxalinyl; or

each R^b is independently (C₃₋₆)cycloalkyl, aryl; aryloxy, benzyloxy, halogen, hydroxy, (C₁₋₆)alkyl, (C₁₋₆)alkoxy, (C₁₋₆)haloalkyl, (C₁₋₆)haloalkoxy, aminosulfonyl,

(C₁₋₆)alkylaminosulfonyl, di-(C₁₋₆)alkylaminosulfonyl, arylaminosulfonyl, oxo, carboxy, cyano, nitro, mono-(C₁₋₅)alkylamino, di-(C₁₋₅)alkylamino, carboxamide, amidino or guanidino; or

R³ and R⁴ in (Ia) or (Ib) together with the atoms to which they are attached form a heterocycloalkyl ring or a heterocycloalkyl ring fused to an aryl or heteroaryl ring provided the heterocyclic rings contain at least an -SO₂- group, wherein said heterocycloalkyl rings are optionally substituted on the aromatic and/or non-aromatic portion of the rings with one, two, or three R^c;

each R^c and R^{4a} is hydrogen, (C₁₋₆)alkyl optionally interrupted by one or two N, O, S, S(O), or S(O)₂ and optionally substituted by 1-2 oxo, amino, hydroxy, halogen, C₁₋₆)alkyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl, thiopyranyl, furanyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl], benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, benzoxazolyl or quinoxalinyl;

halo, alkoxy, alkylthio, hydroxy, carboxy, aryl, aryloxy, aroyl, furanyl, thienyl, pyrrolyl, imidazolyl, pyridinyl, pyrimidinyl, (C₁₋₆)alkanoyl, -C(O)OR^d where (R^d is hydrogen, (C₁₋₆)alkyl, (C₁₋₆)alkoxyalkyl, (C₁₋₆)haloalkyl, (C₃₋₇)cycloalkyl, (C₃₋₇)-cycloalkyl(C₁₋₆)alkyl, heteroaryl, heteroaryl(C₁₋₄)alkyl, aryl, or aryl(C₁₋₆)alkyl), (C₁₋₆)-alkylsulfonyl, aryloxycarbonyl, benzyloxycarbonyl, (C₁₋₆)alkanoylamino, aroylamino, C₁₋₅ alkylthio, arylthio, (C₁₋₆)alkylsulfonylamino, arylsulfonylamino, (C₁₋₆)alkylamino-sulfonyl, arylaminosulfonyl, (C₃₋₆)cycloalkyl and benzyloxy wherein each of the aforementioned group is optionally substituted with halogen, hydroxy, (C₁₋₆)alkyl, (C₁₋₆)alkoxy, (C₁₋₆)-haloalkyl, (C₁₋₆)haloalkoxy, oxo, carboxy, nitrile, nitro, or NH₂C(O)-.

3. (Original) The compound of Claim 2 wherein E is -CHR⁶C(O)R¹⁰ where R⁶ is saturated alkyl, and R¹⁰ is hetero(C₄₋₁₀)aryl optionally substituted with (C₃₋₁₀)cycloalkyl, (C₆₋₁₀)aryl [optionally substituted with -NR²⁸R^{28a}, -OR²⁹, or halo substituted (C₁₋₄) saturated alkyl], hetero(C₅₋₁₀)aryl, (C₁₋₆) saturated alkyl, halo-substituted (C₁₋₄) saturated alkyl, or -X⁸OR²⁹

where X^8 is (C_{1-6}) saturated alkylene, R^{28} and R^{28a} are independently hydrogen or (C_{1-6}) saturated alkyl, R^{29} is hydrogen, (C_{1-6}) saturated alkyl, or halo-substituted (C_{1-6}) saturated alkyl.

4. (Original) The compound of Claim 3 wherein R^1 is $-CH_2X^9$ wherein X^9 is selected from $-X^{10}SR^{33}$, $-X^{10}C(O)NR^{33}R^{33a}$, $-X^{10}S(O)_2R^{34}$, $-X^{10}COR^{34}$, $-X^{10}OR^{33}$, $-R^{35}$, $-X^{10}SR^{35}$, $-X^{10}S(O)_2R^{35}$, $-X^{10}C(O)R^{35}$, or $-X^{10}C(O)NR^{33}R^{35}$ wherein X^{10} is a bond or (C_{1-6}) alkylene; R^{33} and R^{33a} at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl; R^{34} is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl; and R^{35} is (C_{3-10}) cycloalkyl (C_{0-6}) alkyl, hetero (C_{3-10}) cycloalkyl (C_{0-3}) alkyl, (C_{6-10}) aryl (C_{0-6}) alkyl, hetero (C_{5-10}) aryl (C_{0-6}) alkyl, (C_{9-10}) bicycloaryl (C_{0-6}) alkyl or hetero (C_{8-10}) bicycloaryl (C_{0-6}) alkyl wherein within R^1 any alicyclic or aromatic ring is optionally substituted with one, two, or three radicals independently selected from (C_{1-6}) saturated alkyl, benzyl, cyano, halo, halo-substituted (C_{1-4}) saturated alkyl, $-OR^{36}$, or $-R^{38}$ where R^{36} is (C_{1-6}) saturated alkyl or halo-substituted (C_{1-6}) saturated alkyl and R^{38} is (C_{6-10}) aryl and within R^1 any aliphatic moiety is unsubstituted or substituted further by 1 to 2 radicals independently selected from halo; and R^{1a} is hydrogen.

5. (Original) The compound of Claim 3 wherein R^1 is 2-cyclohexylethyl, cyclohexylmethyl, cyclopentylmethyl, 2-cyclopentylethyl, tert-butylmethyl, 1-methylcyclopropylmethyl, 1-methylcyclohexylmethyl, 1-methylcyclopentylmethyl, 1,3-dimethylcyclopentylmethyl, morpholin-4-ylmethyl, 2,2-dimethyl-3-phenylpropyl, 1-benzylcyclopropylmethyl, 2-(1,1-difluoromethoxy)phenylmethanesulfonylmethyl, 2-methylpropylsulfonylmethyl, phenylmethanesulfonylmethyl, pyridin-2-ylmethanesulfonylmethyl, pyridin-4-ylmethanesulfonylmethyl, cyclopropylmethanesulfonylmethyl, pyridin-3-ylmethanesulfonylmethyl, 2,6-difluorophenylmethanesulfonylmethyl, 2,2-difluoro-3-phenylpropyl, 2,2-dichloropropyl, 2,2-dichloro-3-phenylpropyl, 2-pyridin-2-ylsulfonylethyl, 2-phenylsulfonylethyl, 5-bromothiophen-2-ylmethyl, pyridin-4-ylmethyl, 2,2-dichloroethyl, 2,2,2-trichloroethyl, 1,4-dimethylcyclopentylmethyl, morpholin-4-ylmethyl, isopropylmethanesulfonylmethyl, 2-chlorobenzyl, or 4-fluorobenzyl and R^{1a} is hydrogen.

6. (Original) The compound of Claim 4 wherein R³ is (C₁₋₅)alkyl, (C₃₋₆)cycloalkyl, phenyl, benzyl, naphthyl, (C₁₋₃)alkylsulfonyl(C₁₋₃)alkyl, (C₃₋₆)cycloalkylsulfonyl(C₁₋₃)alkyl, arylsulfonyl(C₁₋₃)alkyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, furanyl, thienyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, isoxazolyl, pyrimidinyl, pyrazinyl, pyridazinyl, indolyl, quinolinyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl or amino; wherein R³ is optionally substituted by one, two, or three substituents independently selected from R^a;

each R^a is independently (C₁₋₃)alkyl, cyclopropyl, cyclopentyl, cyclohexyl, phenyl, naphthyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, furanyl, thienyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, (C₁₋₃)alkoxy, (C₁₋₃)alkanoyl, (C₁₋₃)alkanoyloxy, aryloxy, benzyloxy, (C₁₋₃)alkoxycarbonyl, aryloxycarbonyl, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by (C₁₋₃)alkyl, aryl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, thienyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, benzimidazolyl or benzthiazolyl, or

each R^a is independently (C₁₋₃)alkanoylamino, aroylamino, (C₁₋₃)alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by (C₁₋₃)alkyl, aryl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl or piperazinyl, or

each R^a is independently (C₁₋₃)alkoxycarbonylamino, aryloxycarbonylamino, (C₁₋₃)alkylcarbamoyloxy, arylcarbamoyloxy, (C₁₋₃)alkylsulfonylamino, arylsulfonylamino, (C₁₋₃)alkylamino-sulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by (C₁₋₃)alkyl, aryl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl or piperazinyl, or

each R^a is independently halogen, hydroxy, oxo, carboxy, cyano, nitro, carboxamide, amidino, or guanidino, R^a may be further optionally substituted by one, two or

three R^b ; each R^b is independently (C₁₋₃)alkyl, aryl, (C₁₋₃)alkoxy, (C₁₋₃)haloalkyl, (C₁₋₃)haloalkoxy, aryloxy, benzyloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, carboxamide, amidino or guanidino;

R^2 and R^4 are hydrogen; and

R^{4a} is -C(O)OR^d where (R^d is hydrogen, (C₁₋₆)alkyl, (C₁₋₆)alkoxy(C₁₋₆)alkyl, (C₁₋₆)haloalkyl, (C₃₋₇)cycloalkyl, (C₃₋₇)cycloalkyl(C₁₋₆)alkyl, heteroaryl, heteroaryl(C₁₋₆)alkyl, awl, or aryl(C₁₋₆)alkyl).

7. (Original) The compound of Claim 4 wherein R^2 and R^{4a} are hydrogen;

R^3 is (C₁₋₆) saturated alkyl, phenyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, furanyl, thienyl, pyridinyl, or amino; wherein R^3 is optionally substituted by one, two or three R^a where each R^a is independently halo or (C₁₋₆) saturated alkyl; and

R^4 is hydrogen, (C₁₋₆) saturated alkyl, or halogenated alkyl.

8. (Original) The compound of Claim 4 wherein R^2 and R^{4a} are hydrogen and R^3 and R^4 together with the atoms to which they are attached form a 5 or 6 membered heterocycloalkyl ring containing at least an -SO₂- group or a 5 or 6 membered heterocycloalkyl ring containing at least an -SO₂- group and is fused to a phenyl, thienyl, pyrrolyl, or pyridinyl ring optionally independently substituted by one or two R^c .

9. (Original) The compound of Claim 1 wherein:

R^{1a} , R^2 , R^3 and R^{4a} are hydrogen;

R^1 is -CH₂X⁹ wherein X⁹ is selected from -X¹⁰SR³³, -X¹⁰C(O)NR³³R^{33a}, -X¹⁰S(O)₂R³⁴, -X¹⁰COR³⁴, -X¹⁰OR³³, -R³⁵, -X¹⁰SR³⁵, -X¹⁰S(O)₂R³⁵, -X¹⁰C(O)R³⁵, or X¹⁰C(O)NR³³R³⁵ wherein X¹⁰ is a bond or (C₁₋₆)alkylene; R^{33} and R^{33a} at each occurrence independently is hydrogen, (C₁₋₆)alkyl or halo-substituted(C₁₋₆)alkyl; R^{34} is (C₁₋₆)alkyl or halo-

substituted(C₁₋₆)alkyl; and R³⁵ is (C₃₋₁₀)cycloalkyl(C₀₋₆)alkyl, hetero(C₃₋₁₀)cycloalkyl(C₀₋₃)alkyl, (C₆₋₁₀)aryl(C₀₋₆)alkyl, hetero(C₅₋₁₀)aryl(C₀₋₆)alkyl, (C₉₋₁₀)bicycloaryl(C₀₋₆)alkyl or hetero(C₈₋₁₀)bicycloaryl(C₀₋₆)-alkyl wherein within R¹ any alicyclic or aromatic ring is optionally substituted with one, two, or three radicals independently selected from (C₁₋₆) saturated alkyl, benzyl, cyano, halo, halo-substituted(C₁₋₆) saturated alkyl, -OR³⁶, or -R³⁸ where R³⁶ is (C₁₋₆) saturated alkyl or halo-substituted(C₁₋₆) saturated alkyl and R³⁸ is (C₆₋₁₀)aryl and within R¹ any aliphatic moiety is unsubstituted or substituted further by 1 to 2 radicals independently selected from halo;

E is -CHR⁶C(O)R¹⁰ where R⁶ is saturated alkyl, and R¹⁰ is hetero(C₄₋₁₀)aryl optionally substituted with (C₃₋₁₀)cycloalkyl, (C₆₋₁₀)aryl [optionally substituted with -NR²⁸R^{28a}, -OR²⁹, or halo substituted (C₁₋₄) saturated alkyl], hetero(C₅₋₁₀)aryl, (C₁₋₆) saturated alkyl, halo-substituted (C₁₋₄) saturated alkyl, or -X⁸OR²⁹ where X⁸ is (C₁₋₆) saturated alkylene, R²⁸ and R^{28a} are independently hydrogen or (C₁₋₆) saturated alkyl, R²⁹ is hydrogen, (C₁₋₆) saturated alkyl, or halo-substituted (C₁₋₆) saturated alkyl; and

R⁴ is -SO₂R where R is pyranlyl, thiopyranlyl, furanyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, benzoxazolyl, or quinoxalinyl, -SO₂-saturated alkyl, (C₁₋₆) saturated alkyl substituted with a heteroaryl ring defined immediately above or pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, or indolinyl, -SO₂NRR' where R and R' are independently hydrogen or (C₁₋₆) saturated alkyl wherein each of the aforementioned group is optionally substituted with halogen, hydroxy, (C₁₋₆) saturated alkyl, (C₁₋₆) saturated alkoxy, (C₁₋₆) saturated haloalkyl, (C₁₋₆) saturated haloalkoxy, oxo, carboxy, nitrile, nitro or -CONH₂.

10. (Original) The compound of Claim 1 wherein:

R^{1a}, R² and R⁴ are hydrogen;

R¹ is -CH₂X⁹ wherein X⁹ is selected from -X¹⁰SR³³, -X¹⁰C(O)NR³³R^{33a}, -X¹⁰S(O)₂R³⁴, -X¹⁰COR³⁴, -X¹⁰OR³³, -R³⁵, -X¹⁰SR³⁵, -X¹⁰S(O)₂R³⁵, -X¹⁰C(O)R³⁵, or

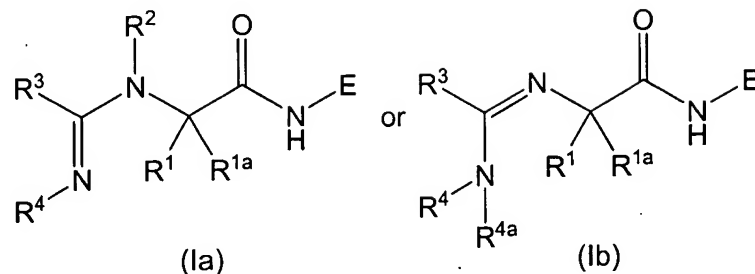
$-X^{10}C(O)NR^{33}R^{35}$ wherein X^{10} is a bond or (C_{1-6}) alkylene; R^{33} and R^{33a} at each occurrence independently is hydrogen, (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl; R^{34} is (C_{1-6}) alkyl or halo-substituted (C_{1-6}) alkyl; and R^{35} is (C_{3-10}) cycloalkyl (C_{0-6}) alkyl, hetero (C_{3-10}) cycloalkyl (C_{0-3}) alkyl, (C_{6-10}) aryl (C_{0-6}) alkyl, hetero (C_{5-10}) aryl (C_{0-6}) alkyl, (C_{9-10}) bicycloaryl (C_{0-6}) alkyl or hetero (C_{8-10}) bicycloaryl (C_{0-6}) -alkyl wherein within R^1 any alicyclic or aromatic ring is optionally substituted with one, two, or three radicals independently selected from (C_{1-6}) saturated alkyl, benzyl, cyano, halo, halo-substituted (C_{1-4}) saturated alkyl, $-OR^{36}$, or $-R^{38}$ where R^{36} is (C_{1-6}) saturated alkyl or halo-substituted (C_{1-6}) saturated alkyl and R^{38} is (C_{1-6}) aryl and within R^1 any aliphatic moiety is unsubstituted or substituted further by 1 to 2 radicals independently selected from halo;

E is $-CHR^6C(O)R^{10}$ where R^6 is saturated alkyl, and R^{10} is hetero (C_{4-10}) aryl optionally substituted with (C_{3-10}) cycloalkyl, (C_{6-10}) aryl [optionally substituted with $-NR^{28}R^{28a}$, $-OR^{29}$, or halo substituted (C_{1-4}) saturated alkyl], hetero (C_{5-10}) aryl, (C_{1-6}) saturated alkyl, halo-substituted (C_{1-4}) saturated alkyl, or $-X^8OR^{29}$ where X^8 is (C_{1-6}) saturated alkylene, R^{28} and R^{28a} are independently hydrogen or (C_{1-6}) saturated alkyl, R^{29} is hydrogen, (C_{1-6}) saturated alkyl, or halo-substituted (C_{1-6}) saturated alkyl;

R^3 is hydrogen, (C_{1-6}) saturated alkyl, phenyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, furanyl, thienyl, pyridinyl, or amino; wherein R^3 is optionally substituted by one, two or three R^a where R^a is halo or (C_{1-6}) saturated alkyl; and

R^{4a} is heteroaryl, (C_{1-6}) saturated alkylsulfonyl, or (C_{1-6}) halo-substituted saturated alkylsulfonyl.

11. (Original) A compound of Formula (Ia) or (Ib):



wherein:

R^{1a} , R^2 and R^{4a} are hydrogen;

E is $-\text{CHR}^6\text{C}(\text{O})\text{R}^{10}$ where R^6 is ethyl, propyl, or butyl, and R^{10} is hetero(C_{4-10})aryl optionally substituted with (C_{3-10})aryl, (C_{6-10})aryl; hetero(C_{5-10})aryl, (C_{1-6})alkyl, halo, halo-substituted (C_{1-4})alkyl, $\text{NR}^{28}\text{R}^{28a}$, $-\text{OR}^{29}$, or $-\text{COOR}^{28}$, $-\text{COR}^{29}$ where R^{28} and R^{28a} are independently hydrogen or $-(\text{C}_{1-6})$ alkyl, R^{29} is hydrogen, $-(\text{C}_{1-6})$ alkyl, or halo-substituted $-(\text{C}_{1-6})$ alkyl;

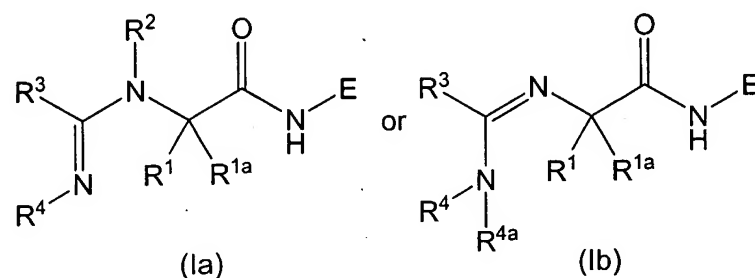
R^1 is 2,2-dichloroethyl, 2,2,2-trichloroethyl, isopropylmethanesulfonylmethyl, 2,2-difluoro-3-phenylpropyl, 2,2-dichloro-3-phenylpropyl, 2-cyclohexylethyl, cyclohexylmethyl, cyclopentylmethyl, 2-cyclopentylethyl, *tert*-butylmethyl, 1-methylcyclopropylmethyl, 1-methylcyclohexylmethyl, 1-methylcyclopentylmethyl, 1,3-dimethylcyclopentylmethyl, morpholin-4-ylmethyl, 2,2-dimethyl-3-phenylpropyl, 1-benzylcyclopropylmethyl, 2-(1,1-difluoromethoxy)phenylmethanesulfonylmethyl, 2-methylpropylsulfonylmethyl, phenylmethanesulfonylmethyl, pyridin-2-ylmethanesulfonyl-methyl, pyridin-4-ylmethanesulfonylmethyl, cyclopropylmethanesulfonylmethyl, pyridin-3-ylmethanesulfonylmethyl; 2,6-difluorophenylmethanesulfonylmethyl, 2,2-dichloropropyl, 2-pyridin-2-ylsulfonylethyl, 2-phenylsulfonylethyl, 5-bromothien-2-ylmethyl, pyridin-4-ylmethyl, 2-chlorobenzyl, or 4-fluorobenzyl;

R^3 is hydrogen, (C_{1-6}) saturated alkyl, phenyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, furanyl, thienyl, pyridinyl, or amino; wherein R^3 is

optionally substituted by one, two or three R^a where each R^a is independently halo or (C_{1-6}) saturated alkyl; and

R^4 is hydrogen, (C_{1-6}) saturated alkyl, halo-substituted saturated alkyl, or (C_{1-6}) saturated alkylsulfonyl.

12. (Original) A compound of Formula (Ia) or (Ib):



wherein:

R^{1a} , R^2 and R^{4a} are hydrogen;

E is $-CH(R^6)C(O)R^{10}$ where R^6 ethyl and R^{10} is benzoxazol-2-yl, oxazolo[4,5-b]pyridin-2-yl, 2-pyridin-3-yl-[1,3,4]-oxadiazol-5-yl, 2-pyridin-4-yl-[1,3,4]-oxadiazol-5-yl, 2-ethyl-[1,3,4]-oxadiazol-5-yl, 2-isopropyl-[1,3,4]-oxadiazol-5-yl, 2-*tert*-butyl-[1,3,4]-oxadiazol-5-yl, 2-phenyl-[1,3,4]-oxadiazol-5-yl, 2-methoxymethyl-[1,3,4]-oxadiazol-5-yl, 2-furan-2-yl-[1,3,4]-oxadiazol-5-yl, 2-thien-2-yl-[1,3,4]-oxadiazol-5-yl, 2-(4-methoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(2-methoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(3-methoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(2-trifluoromethoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(3-trifluoromethoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(4-trifluoromethoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(4-dimethylaminophenyl)-[1,3,4]-oxadiazol-5-yl, pyradizin-3-yl, pyrimidin-2-yl, 3-phenyl-[1,2,4]-oxadiazol-5-yl, 3-ethyl-[1,2,4]-oxadiazol-5-yl, 3-cyclopropyl-[1,2,4]-oxadiazol-5-yl, 3-thien-3-yl-[1,2,4]-oxadiazol-5-yl, 3-pyridin-4-yl-[1,2,4]-oxadiazol-5-yl, 3-pyridin-2-yl-[1,2,4]-oxadiazol-5-yl, 5-ethyl-[1,2,4]-oxadiazol-3-yl, 5-phenyl-[1,2,4]-oxadiazol-3-yl, 5-thien-3-yl-[1,2,4]-oxadiazol-3-yl, 5-trifluoromethyl-[1,2,4]-oxadiazol-3-yl, 5-pyridin-4-yl-[1,2,4]-oxadiazol-3-yl, or 5-phenyloxazol-2-yl;

2,2-dichloroethyl, 2,2,2-trichloroethyl, isopropylmethanesulfonylmethyl, 2,2-difluoro-3-phenylpropyl, 2,2-dichloro-3-phenylpropyl, 2-cyclohexylethyl, cyclohexylmethyl, cyclopentylmethyl, 2-cyclopentylethyl, *tert*-butylmethyl, 1-methylcyclopropylmethyl, 1-methylcyclohexylmethyl, 1-methylcyclopentylmethyl, 1,3-dimethylcyclopentylmethyl, morpholin-4-ylmethyl, 2,2-dimethyl-3-phenylpropyl, 1-benzylcyclopropylmethyl, 2-(1,1-difluoromethoxy)phenylmethanesulfonylmethyl, 2-methylpropylsulfonylmethyl, phenylmethanesulfonylmethyl, pyridin-2-ylmethanesulfonyl-methyl, pyridin-4-ylmethanesulfonylmethyl, cyclopropylmethanesulfonylmethyl, pyridin-3-ylmethanesulfonylmethyl, 2,6-difluorophenylmethanesulfonylmethyl, 2,2-dichloropropyl, 2-pyridin-2-ylsulfonylethyl, 2-phenylsulfonylethyl, 5-bromothien-2-ylmethyl, pyridin-4-ylmethyl, 2-chlorobenzyl, or 4-fluorobenzyl;

R³ is methyl, trifluoromethyl, 2,2,2-trifluoroethylamino, amino, *N,N*-dimethylamino, morpholin-4-yl, pyrrolidin-1-yl, piperidin-1-yl, 4-methylpiperazin-1-yl, thien-2-yl, thien-3-yl, furan-2-yl, furan-3-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-5-yl, pyrimidin-4-yl, oxazol-4-yl, oxazol-5-yl, thiazol-4-yl, thiazol-5-yl, quinolin-6-yl, indol-5-yl, 2-methylimidazol-4-yl, phenyl, or 4-fluorophenyl; and

R⁴ is hydrogen, 2,2,2-trifluoroethyl, methyl, or methylsulfonyl.

13. (Original) The compound of Claim 11 wherein R⁴ is 2,2,2-trifluoroethyl.

14. (Original) The compound of Claim 12 wherein R⁴ is 2,2,2-trifluoroethyl.

15. (Original) The compound of Claim 1 wherein:

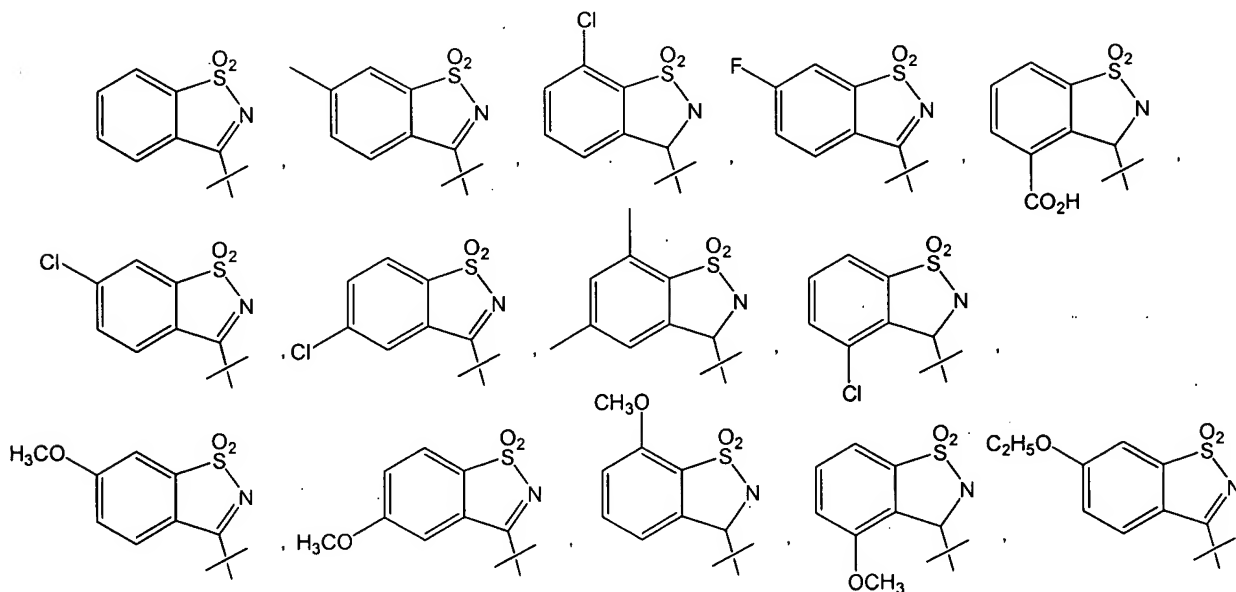
R^{1a}, R² and R^{4a} are hydrogen;

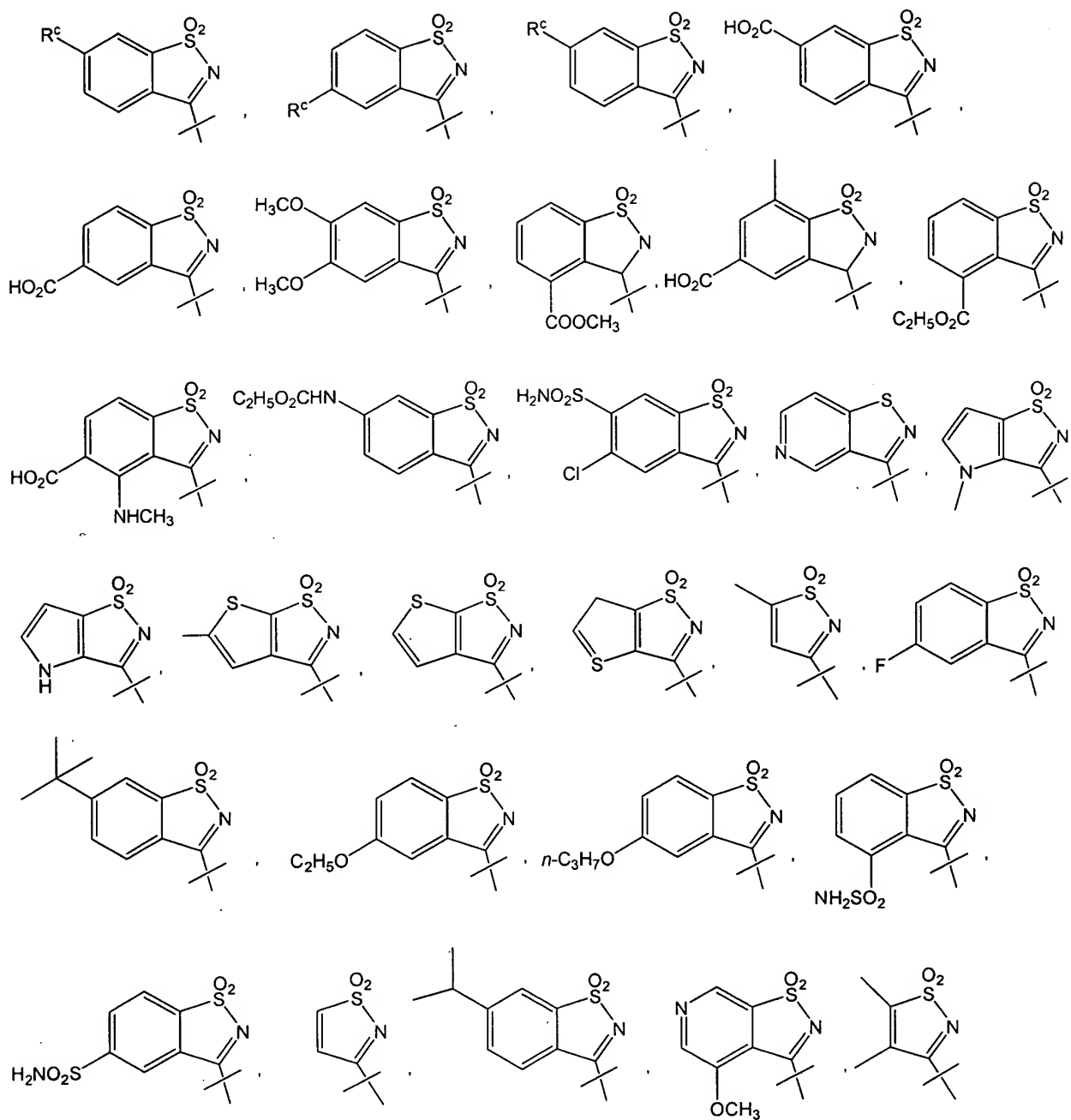
E is -CHR⁶C(O)R¹⁰ where R⁶ is saturated alkyl, and R¹⁰ is hetero(C₄₋₁₀)aryl optionally substituted with (C₃₋₁₀)cycloalkyl, (C₆₋₁₀)aryl [optionally substituted with -NR²⁸R^{28a}, -OR²⁹, or halo substituted (C₁₋₄) saturated alkyl], hetero(C₅₋₁₀)aryl, (C₁₋₆) saturated alkyl, halo-substituted (C₁₋₄) saturated alkyl, or -X⁸OR²⁹ where X⁸ is (C₁₋₆) saturated alkylene, R²⁸ and R^{28a}

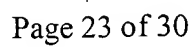
are independently hydrogen or (C₁₋₆) saturated alkyl, R²⁹ is hydrogen, (C₁₋₆) saturated alkyl, or halo-substituted (C₁₋₆) saturated alkyl;

R¹ is -CH₂X⁹ wherein X⁹ is selected from -X¹⁰SR³³, -X¹⁰C(O)NR³³R^{33a}, X¹⁰S(O)₂R³⁴, -X¹⁰COR³⁴, -X¹⁰OR³³, -R³⁵, -X¹⁰SR³⁵, -X¹⁰S(O)₂R³⁵, -X¹⁰C(O)R³⁵, or X¹⁰C(O)NR³³R³⁵ wherein X¹⁰ is a bond or (C₁₋₆)alkylene; R³³ and R^{33a} at each occurrence independently is hydrogen, (C₁₋₆)alkyl or halo-substituted(C₁₋₆)alkyl; R³⁴ is (C₁₋₆)alkyl or halo-substituted(C₁₋₆)alkyl; and R³⁵ is (C₃₋₁₀)cycloalkyl(C₀₋₆)alkyl, hetero(C₃₋₁₀)cycloalkyl(C₀₋₃)alkyl, (C₆₋₁₀)aryl(C₀₋₆)alkyl, hetero(C₅₋₁₀)aryl(C₀₋₆)alkyl, (C₉₋₁₀)bicycloaryl(C₀₋₆)alkyl or hetero(C₈₋₁₀)bicycloaryl(C₀₋₆)-alkyl wherein within R¹ any alicyclic or aromatic ring is optionally substituted with one, two, or three radicals independently selected from (C₁₋₆) saturated alkyl, benzyl, cyano, halo, halo-substituted(C₁₋₄) saturated alkyl, -OR³⁶, or -R³⁸ where R³⁶ is (C₁₋₆) saturated alkyl or halo-substituted(C₁₋₆) saturated alkyl and R³⁸ is (C₆₋₁₀)aryl and within R¹ any aliphatic moiety is unsubstituted or substituted further by 1 to 2 radicals independently selected from halo; and

R³ and R⁴ together with the atoms to which they are attached form a group selected from:







where R^c is amino, methylsulfonylamino, ethylsulfonylamino, methylamino, dimethylamino, acetyl amino, methoxy, ethoxy, methylaminocarbonyl, aminocarbonyl, diethylaminocarbonyl, dimethylaminocarbonyl, methylaminocarbonyl, ureido, or ethoxycarbonylamino.

16. (Original) The compound of Claim 15 wherein R¹ is 2,2-dichloroethyl, 2,2,2-trichloroethyl, isopropylmethanesulfonylmethyl, 2,2-difluoro-3-phenylpropyl, 2,2-dichloro-3-phenylpropyl, 2-cyclohexylethyl, cyclohexylmethyl, cyclopentylmethyl, 2-cyclopentylethyl, *tert*-butylmethyl, 1-methylcyclopropylmethyl, 1-methylcyclohexylmethyl, 1-methylcyclopentylmethyl, 1,3-dimethylcyclopentylmethyl, morpholin-4-ylmethyl, 2,2-dimethyl-3-phenylpropyl, 1-benzylcyclopropylmethyl, 2-(1,1-difluoromethoxy)phenylmethanesulfonylmethyl, 2-methylpropylsulfonylmethyl, phenylmethanesulfonylmethyl, pyridin-2-ylmethanesulfonyl-methyl, pyridin-4-ylmethanesulfonylmethyl, cyclopropylmethanesulfonylmethyl, pyridin-3-ylmethanesulfonylmethyl, 2,6-difluorophenylmethanesulfonylmethyl, 2,2-dichloropropyl, 2-pyridin-2-ylsulfonylethyl, 2-phenylsulfonylethyl, 5-bromothiophen-2-ylmethyl, pyridin-4-ylmethyl, 2-chlorobenzyl, or 4-fluorobenzyl.

17. (Original) The compound of Claim 16 wherein R⁶ ethyl and R¹⁰ is benzoxazol-2-yl, oxazolo[4,5-b]pyridin-2-yl, 2-pyridin-3-yl-[1,3,4]-oxadiazol-5-yl, 2-pyridin-4-yl-[1,3,4]-oxadiazol-5-yl, 2-ethyl-[1,3,4]-oxadiazol-5-yl, 2-isopropyl-[1,3,4]-oxadiazol-5-yl, 2-*tert*-butyl-[1,3,4]-oxadiazol-5-yl, 2-phenyl-[1,3,4]-oxadiazol-5-yl, 2-methoxymethyl-[1,3,4]-oxadiazol-5-yl, 2-furan-2-yl-[1,3,4]-oxadiazol-5-yl, 2-thien-2-yl-[1,3,4]-oxadiazol-5-yl, 2-(4-methoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(2-methoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(3-methoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(2-trifluoromethoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(3-trifluoromethoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(4-trifluoromethoxyphenyl)-[1,3,4]-oxadiazol-5-yl, 2-(4-dimethylaminophenyl)-[1,3,4]-oxadiazol-5-yl, pyridazin-3-yl, pyrimidin-2-yl, 3-phenyl-[1,2,4]-oxadiazol-5-yl, 3-ethyl-[1,2,4]-oxadiazol-5-yl, 3-cyclopropyl-[1,2,4]-oxadiazol-5-yl, 3-thien-3-yl-[1,2,4]-oxadiazol-5-yl, 3-pyridin-4-yl-[1,2,4]-oxadiazol-5-yl, 3-pyridin-2-yl-[1,2,4]-oxadiazol-5-yl, 5-ethyl-[1,2,4]-oxadiazol-3-yl, 5-phenyl-[1,2,4]-oxadiazol-3-

yl, 5-thien-3-yl-[1,2,4]-oxadiazol-3-yl, 5-trifluoromethyl-[1,2,4]-oxadiazol-3-yl, 5-pyridin-4-yl-[1,2,4]-oxadiazol-3-yl, or 5-phenyloxazol-2-yl.

18. (Original) A pharmaceutical composition pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1, individual isomer or mixture of isomers thereof, or a pharmaceutically acceptable salt thereof, in admixture with one or more suitable excipients.

19. (Original) A pharmaceutical composition pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 11, individual isomer or mixture of isomers thereof, or a pharmaceutically acceptable salt thereof, in admixture with one or more suitable excipients.

20. (Original) A pharmaceutical composition pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 12, individual isomer or mixture of isomers thereof, or a pharmaceutically acceptable salt thereof, in admixture with one or more suitable excipients.

21. (Original) A pharmaceutical composition pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 13, individual isomer or mixture of isomers thereof, or a pharmaceutically acceptable salt thereof, in admixture with one or more suitable excipients.

22. (Original) A pharmaceutical composition pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 14, individual isomer or mixture of isomers thereof, or a pharmaceutically acceptable salt thereof, in admixture with one or more suitable excipients.

23. (Original) A method for treating a disease in an animal mediated by cysteine proteases, in particular cathepsin K, S, or F, which method comprises administering to the animal a pharmaceutical composition pharmaceutical composition comprising a therapeutically effective

amount of a compound of Claim 1, individual isomer or mixture of isomers thereof, or a pharmaceutically acceptable salt thereof, in admixture with one or more suitable excipients.

24. (Original) A method for treating a disease in an animal mediated by Cathepsin S which method comprises administering to the animal a pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 11, individual isomer or mixture of isomers thereof, or a pharmaceutically acceptable salt thereof, in admixture with one or more suitable excipients.

25. (Original) A method for treating a disease in an animal mediated by Cathepsin S which method comprises administering to the animal a pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 12, individual isomer or mixture of isomers thereof, or a pharmaceutically acceptable salt thereof, in admixture with one or more suitable excipients.

26. (Original) The method of Claim 23 wherein the disease is psoriasis.

27. (Original) The method of Claim 25 wherein the disease is psoriasis.